

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
30 January 2003 (30.01.2003)

PCT

(10) International Publication Number
WO 03/007938 A1

(51) International Patent Classification: **A61K 31/34**,
31/56, 31/70, 31/355

(21) International Application Number: PCT/US02/21883

(22) International Filing Date: 10 July 2002 (10.07.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/306,277 17 July 2001 (17.07.2001) US

(71) Applicant (*for all designated States except US*): AIDAN,
INC. [US/US]; 621 S. 48th Street, Suite 111, Tempe, AZ
85281 (US).

(72) Inventor; and

(75) Inventor/Applicant (*for US only*): RIORDAN, Neil, H.
[US/US]; 6041 W. Shannon Street, Chandler, AZ 85226
(US).

(74) Agent: BENEDICT, Mark, R.; Knobbe, Martens, Olson
& Bear, LLP, 620 Newport Center Drive, 16th Floor, New-
port Beach, CA 92660 (US).

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU,
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,
CZ (utility model), CZ, DE (utility model), DE, DK (utility
model), DK, DM, DZ, EC, EE (utility model), EE, ES, FI
(utility model), FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,
IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,
LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM,
PH, PL, PT, RO, RU, SD, SE, SG, SI, SK (utility model),
SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZM, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM,
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),
Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK,
TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
GW, ML, MR, NE, SN, TD, TG).

Declaration under Rule 4.17:

— *of inventorship (Rule 4.17(iv)) for US only*

Published:

— *with international search report*

*For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*

(54) Title: METHOD FOR THE TREATMENT OF ATOPIC DERMATITIS

(57) Abstract: A method for treating the symptoms of atopic dermatitis is presented by treating the area topically or systemically with an anti-mycoplasma agent or antibiotic, such as tetracycline or erythromycin.



WO 03/007938 A1

METHOD FOR THE TREATMENT OF ATOPIC DERMATITIS

FIELD OF THE INVENTION

5

This invention relates to a method for the treatment of atopic dermatitis using an anti-mycoplasma antibiotic.

BACKGROUND OF THE INVENTION

10

Atopic dermatitis (also called atopic eczema) is a common inflammatory skin disorder characterized by a chronic relapsing course. One person in 10 has the disease at some time in their life, usually in childhood. Atopic is a term used to describe allergic conditions such as asthma, hayfever, and atopic dermatitis. People with atopic dermatitis usually have dry, itchy and easily irritated skin. This can continue for years and may result in damage to the skin. The exact cause is

15

not known, although there is some relation to asthma, hayfever, and food allergies. Other skin infections may be associated with the disease such as impetigo, athlete's foot, and herpes.

Previously, an autoimmune etiology was believed to be the cause of atopic dermatitis and immunosuppressive treatments such as hydrocortisone, were used with minimal success. Therefore, an effective treatment for atopic dermatitis is needed.

20

SUMMARY OF THE INVENTION

25

One object of the invention is to provide a pharmaceutical consisting of any anti-mycoplasma agent for the treatment of atopic dermatitis. The agents may be any antibiotic or other agent which is effective against mycoplasma, for example, any antibiotic selected from the group consisting of inhibitors of protein synthesis, inhibitors of metabolism, inhibitors of plasma membrane function or synthesis. The antibiotic or agent may be applied topically or systemically. The topical agent may be in a cream or lotion and may include other pharmaceuticals. The topical treatment may also include chemicals which contribute to the healing of the dermatitis or

30

associated pathologies, such as anti-oxidants, immunosuppressants, other antibiotics and moisturizers.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

A method for the treatment of atopic dermatitis is provided which comprises systemically or topically applying an anti-mycoplasma agent to the patient or the affected area. The method results from the finding that when skin cells from the affected area of a patient were removed and treated with a fluorescent nucleic acid stain, microscopic examination revealed a staining of small bodies associated with the cell membranes of the cells, like that seen with mycoplasma infected tissue culture cells. As a result, the patient was treated with an antibiotic used for the treatment of mycoplasma infections and the patient experienced a complete reversal of symptoms.

Atopic dermatitis (also called atopic eczema) is a common skin disorder characterized by a chronic relapsing course. One person in 10 has the disease at some time in their life, usually in childhood. Atopic is a term used to describe allergic conditions such as asthma, hayfever, and atopic dermatitis. People with atopic dermatitis usually have dry, itchy and easily irritated skin. This can continue for years and may result in damage to the skin. The exact cause is unknown, although there is some relation to asthma, hayfever, and food allergies and the cause is thought to be autoimmune. Other skin infections may be associated with the disease such as impetigo, athlete's foot, and herpes.

However, the results presented herein suggest that antibiotics which are typically used to treat Mycoplasma can also be used to treat atopic dermatitis. This, plus the microscopic evidence, suggests that Mycoplasma may be involved in the etiology or symptoms of the disease.

Mycoplasma are bacteria that do not form cell walls and are therefore pleomorphic. Mycoplasma are the smallest known bacteria that can grow and reproduce outside of a living cell (0.1 to 2.5 μ m). Their plasma membranes contain sterols, making them unusual among the other bacteria groups. Because they do not have cell walls, antibiotics which target cell walls are not effective in treating them. The mycoplasma has an affinity for plasma membranes, so when looking at tissue culture cells or smears, mycoplasma can be identified by staining with fluorescent nucleic acid stains and noting small bodies staining over the cell surface.

Antibiotics or antimicrobial agents

Antibiotics such as penicillins and cephalosporins are not useful against mycoplasma. However, antibiotics such as tetracycline and related antibiotics such as doxycycline are effective as are erythromycins and related antibiotics. Therefore, it is envisioned that any antibiotic or agent which is effective against mycoplasma can be used to treat atopic dermatitis. This includes antibiotics such as inhibitors of protein synthesis, inhibitors of bacterial metabolism, inhibitors of membrane activity and synthesis, and inhibitors of nucleic acid synthesis.

Typically, the first line antibiotic for treatment of Mycoplasma infection is Erythromycin and doxycycline. The second line is azithromycin and clarithromycin. However, this is for the

treatment of pneumonia and Urinary tract infections. It is envisioned that the range of antibiotics as well as those that are most efficacious may vary depending on the site of action and the method of administration. However, the following antibiotic groups are useful for the treatment of mycoplasma infections and therefore, useful for the treatment of atopic dermatitis.

5 The antibiotics for use in the presently claimed invention may be selected from one of the following groups or may be a mixture of at least two antibiotics from the following groups. For example, a bacteriostatic and a bacteriocidal antibiotic may be mixed. In particular, those antibiotics which have a synergistic effect may be used.

Inhibition of cell wall synthesis

10 These antibiotics include the penicillins and cephalosporins and would be unlikely to be effective for the treatment of mycoplasma because mycoplasma do not contain a cell wall.

Inhibition of protein synthesis

15 These antibiotics inhibit protein synthesis and include the aminoglycosides (Streptomycins), the tetracyclines (doxycycline and minocycline), chloramphenicol, and the macrolides (erythromycin).

 Examples of related antibiotics which also act by inhibiting protein synthesis include Chloramphenicol, Erythromycin, lincomycins, aminoglycosides, Amikacin, Gentamicin, Kanamycin, Neomycin, Netilmicin, Streptomycin, and Tobramycin.

Inhibition of Nucleic Acid Synthesis

20 These antibiotics interfere with the processes of DNA replication and transcription in microorganisms. These antibiotics include the rifamycins, quinolones, and fluoroquinolones, such as norfloxacin, and rifampin. Other antibiotics which have this mode of action which may be used include Nalidixic acid, Novobiocin, Pyrimethamine, rifampin, Sulfonamides, and Trimethoprim. Alternatively, Gatifloxacin, a new fluoroquinone, has been found to be effective against
25 mycoplasma at a dose of about 400mg orally or iv.

Injury to the Plasma Membrane

 Typically, these antibiotics, such as Polymyxin B and Bacitracin bring about changes in the permeability of the plasma membrane. Some antifungal drugs, such as amphotericin B, miconazole and ketoconazole combine with sterols in the plasma membrane to disrupt the membrane.

30 Because the cell membrane of the mycoplasma contains sterols, antibiotics which are typically active against the fungal cell membrane, such as polyenes may be effective. Other antibiotics active against bacterial cell membranes such as polymyxins, amphotericin B, colistin, imidazoles, Nystatin, and Polymyxins may be useful.

Inhibiting the Synthesis of Essential Metabolites

35 These antibiotics inhibit essential metabolites and include the sulfanilamides.

Other treatments

Other treatments such as (S0-(-)-9-fluoro-2,3-dihydro-3-methyl-10-[4-(2-pyridyl)-1-piperazinyl]-7H-pyrido[1,2,3-de][1,4]benzoxazine-6-carboxylic acid (YH-6) (Ye et al. Zhongguo Yao Li Xue Bao, 1999 Nov.; 20(11):1031-4) have been found to be effective against mycoplasma infections.

Example of antibiotics known to be effective against mycoplasma include the following: doxycycline, erythromycin, polyenes, polymyxins, amphotericin B, colistin, imidazoles, Nystatin, Polymyxins, Chloramphenicol, lincomycins, aminoglycosides, Amikacin, Gentamicin, Kanamycin, Neomycin, Netilmicin, Streptomycin, Tobramycin, Nalidixic acid, Novobiocin, Pyrimethamine, rifampin, Sulfonamides, azithromycin, clarithromycin, moxifloxacin, trovafloxacin, enrofloxacin, levofloxacin, ofloxacin, ciprofloxacin, fleroxacin, clinafloxacin, josamycin, tylosin, spiramycin, kitasamycin, kanamycin, toxithromycin, dirithromycin, chloramphenicol, thiamphenicol, tiamulin, oxytetracycline, chlortetracycline, grepafloxacin, Trimethoprim, (S0-(-)-9-fluoro-2,3-dihydro-3-methyl-10-[4-(2-pyridyl)-1-piperazinyl]-7H-pyrido[1,2,3-de][1,4]benzoxazine-6-carboxylic acid (YH-6), and Gatifloxacin.

It is envisioned that any newly developed antibiotics or treatments which are found to be effective against mycoplasma or which fit into one of the classifications above can be used effectively for the treatment of atopic dermatitis.

It is envisioned that many of the newly isolated or developed antibiotics may be more active against mycoplasma and therefore particularly useful for the methods disclosed. For example, grepafloxacin has been found to be four-fold more active against mycoplasma than ofloxacin. Trovafloxacin was found to be more active than doxycycline and erythromycin. In addition macrolides such as tylosin and tilmicosin, aminoglycosides and aminocyclitol classes such as gentamicin and spectinomycin are active against mycoplasma. These compounds were considerably more active than trimethoprim/sulfamethaxazole and erythromycin. Levofloxacin showed greater activity against *M. hominis* compared with ofloxacin, ciprofloxacin, fleroxacin, doxycycline and erythromycin.

Therefore, any of the above antibiotics can be used to treat atopic dermatitis, including derivatives, pharmaceutically acceptable salts, and combinations. As used herein, the term "pharmaceutically-acceptable salts or complexes" refers to salts or complexes that retain the desired biological activity of the parent compound and exhibit minimal, if any, undesired toxicological effects. Examples of such salts are (a) acid addition salts formed with inorganic acids (for example, hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, nitric acid, and the like), salts formed with organic acids such as acetic acid, oxalic acid, tartaric acid, succinic acid, malic acid, ascorbic acid, benzoic acid, tannic acid palmoic acid, alginic acid, polyglutamic

acid, naphthalenesulfonic acids, naphthalenedisulfonic acids, and polygalacturonic acid, and salt formed from fatty acids such as myristic acid, palmitic acid, stearic acid, palmitoleic acid, oleic acid, linoleic acid and linolenic acid; (b) base addition salts formed with polyvalent metal cations such as zinc, calcium, bismuth, barium, magnesium, aluminum, copper, cobalt, nickel, cadmium, and the like, or with an organic cation forming from N,N-dibenzylethylene-diamine or ethylenediamine; or (c) combinations of (a) and (b); e.g., a zinc tannate salt or the like.

Derivatives include any anti-mycoplasma antibiotics which can be modified in order to enhance their usefulness as pharmaceutical compositions. For example, an alteration of charge to affect water and lipid solubility and thus alter the potential for percutaneous adsorption is a derivative and decrease side effects or irritancy. The vehicle or carrier, can also be modified to enhance the uptake and/or effects of the composition.

Dosages and formulations

Topical administration is preferred because the chances of side effects are reduced and the antibiotic can be applied only to the effected area. Topical dosages for the treatment of atopic dermatitis will also vary depending on the antibiotic used and the length of time for which the antibiotic may be used. However, dosages are well known to one of skill in the art and can be identified using a pharmacology reference book. For example, for doxycycline, a typical treatment provides a cream to cover the affected area liberally, the cream is a preparation comprising 10 or more mg/1.5ml cream two times daily until symptoms are reduced or disappear. In a further embodiment, a sufficient amount of a preparation comprising 50 mg/1.5 ml is used to cover the affected area two times daily until symptoms disappear. In a further embodiment, a sufficient amount of a preparation comprising 100 mg/1.5 ml is used two times daily until symptoms disappear. In one embodiment, the amount sufficient to cover the affected area is about 100 μ l to 1 ml. In a further embodiment, the amount sufficient to cover the affected area is about 100 μ l to 300 μ l. However, it is understood to one of skill in the art that the concentration of antibiotic can vary depending on the number of times a day it is applied and the amount will vary depending on the size of the affected area. In addition, a lower concentration may be used for a longer period of time to effect disappearance or reduction of symptoms. In addition, a higher concentration can be used. However, the effectiveness of the antibiotic will plateau at a certain concentration and any higher concentration of antibiotic will be superfluous. In addition, substances may be added such as a pharmaceutically-acceptable diluent, or carrier other than or in addition to a lotion. Substances may also be added which speed the healing process of the skin, which treat other symptoms (such as itching), and/or which make the cream or gel easier and more pleasant to apply. Examples of such substances which may speed healing include but are not limited to: vitamin E oil, vitamin C,

retinoic acid, antioxidants, hydrocortisone, carnosine etc. In addition, lotions may be added as well as artificial colors and perfumes.

In addition to all of the other materials listed above, thickening agents, emollients, and stabilizers can be used to prepare topical compositions. Examples of thickening agents include petrolatum beeswax, xanthan gum, or polyethylene glycol, humectants such as sorbitol, emollients such as mineral oil, lanolin and its derivatives, or squalene. A number of solutions and ointments are commercially available. Skin penetration enhancers may also be included or alternatively, the pharmaceutical may be made up in a vesicle or other type of skin penetration enhancer.

Systemic dosages for the treatment of atopic dermatitis will vary depending on the antibiotic used. However, dosages are set forth in many reference books, including the physician's desk reference or are well known to one of skill in the art. Oral compositions will generally include an inert diluent or an edible carrier. They may be enclosed in gelatin capsules or compressed into tablets. For the purpose of oral therapeutic administration, the active compound can be incorporated with excipients and used in the form of tablets, troches, or capsules. Pharmaceutically compatible binding agents, and/or adjuvant materials can be included as part of the composition.

The tablets, pills, capsules, troches and the like can contain any of the following ingredients or compounds of a similar nature: a binder such as microcrystalline cellulose, gum tragacanth or gelatin; an excipient such as starch or lactose, a disintegrating agent such as alginic acid, Primogel, or corn starch; a lubricant such as magnesium stearate or Sterotes; a glidant such as colloidal silicon dioxide; a sweetening agent such as sucrose or saccharin; or a flavoring agent such as peppermint, methyl salicylate, or orange flavoring.

When the dosage unit form is a capsule, it can contain, in addition to material of the above type, a liquid carrier such as a fatty oil. In addition, dosage unit forms can contain various other materials which modify the physical form of the dosage unit, for example, coatings of sugar, shellac, or other enteric agents. Alternatively, the dosage form may be a unit of liquid, such as an elixir, suspension, syrup, wafer, or chewing gum.

Administration may be systemically or topically. Systemic administration includes orally, intravenously, subcutaneously, intraperitoneally, intramuscularly, parenterally, submucosally, by inhalation, intranasally, transdermally via a slow release patch, or topically, in an effective dosage range to reduce, treat or cure the atopic dermatitis.

Whether topical or systemic, the mycoplasma antibiotic or chemotherapeutic agent can be mixed with other active materials which do not impair the desired action, or with materials that supplement the desired action, such as other antibiotics, antifungals, anti-inflammatories, antivirals, or other immunosuppressive agents.

Methods of diagnosis of atopic dermatitis

A method for diagnosing a skin disease as atopic dermatitis and, thus, as a disease which would be effectively treated using an anti-mycoplasma agent is presented. The method involves the identification of the presence of mycoplasma in the effected area. The method of identification of mycoplasma can be by any technique known to one of skill in the art, but includes treatment of a scraping or biopsy with a nucleic acid intercolator and microscopic visualization. The visualization may be using a fluorescence microscope. Alternatively, the mycoplasma may be identified using a publicly available kit, by PCR of a mycoplasma specific gene, by RT-PCR of a mycoplasma-specific message, by culture of the organism, or by treating the effected area with an anti-mycoplasma agent and noting a reduction of the symptoms.

Below are examples of specific embodiments for carrying out the present invention. The examples are offered for illustrative purposes only, and are not intended to limit the scope of the present invention in any way.

EXAMPLE 1**Microscopic Examination of the Affected Area**

Cells from the affected area of the hand from a patient diagnosed with atopic dermatitis were removed by scraping and applied to a microscope slide. A smear was made using a DNA-specific dye. Microscopic Examination revealed the presence of mycoplasma on White Blood Cells and Red Blood Cells from the scraping, suggesting that mycoplasma is involved in the symptoms and possible etiology of the disease. In particular that fact that "spots" of staining were seen on the surface of Red Blood Cells was a surprising result because Red Blood Cells do not contain DNA.

In Example 2, a topical solution was produced.

EXAMPLE 2**Topical Solution for the Treatment of Atopic Dermatitis**

100 milligrams of doxycycline was added to 1.5 fluid ounces of a topical cream producing a 100mg/1.5 oz solution

In Examples 3-5, a number of patients were treated with antibiotics which are effective for treating mycoplasma infections.

EXAMPLE 3**Identification of the Presence of Mycoplasma**

A scraping from the affected area of the hand of a male patient aged 41 with chronic atopic dermatitis was taken. The cells were applied to a microscope slide and treated with a DNA-

specific dye, acridine orange. The slide was microscopically examined using a fluorescence microscope fitted with an FITC filter set. Some of the white blood cells and, in particular, the red blood cells from the smear were stained. The stain appeared as small dots over the surface of the cells, typical of a mycoplasma infection. This, then suggested the presence of mycoplasma which
5 bind to the outside of cells upon infection.

EXAMPLE 4

Treatment of a Chronic Case of Atopic Dermatitis

A male patient age 41 had atopic dermatitis for more than 20 years. The patient had been
10 treated over that time with a number of immunosuppressive pharmaceuticals with no effect. The patient began treatment with the cream described in Example 2 and applied the cream topically two times a day. After 3 days, the dermatitis was almost completely gone. The patient continued treatment for 2 weeks. After 3 years with no further treatment the dermatitis returned. However, the large time between infections, suggested a second infection rather than a re-emergence of the
15 first infection. The second infection was again treated with the topical cream in Example 2 and again the dermatitis disappeared by the first week of treatment.

EXAMPLE 5

Effective treatment of a female patient with atopic dermatitis of the face

A female patient aged 31 had atopic dermatitis of the face for more than 5 years. The
20 patient had been treated over that time with a number of immunosuppressive pharmaceuticals with no effect. The patient began treatment with the cream described in Example 2 and applied the cream topically for 6 weeks. After 6 weeks a complete improvement was noted.

EXAMPLE 6

Effective treatment of patients with other anti-mycoplasma agents

A patient with atopic dermatitis is treated with Erythromycin in a formulation of
100 milligrams of Erythromycin/1.5 fluid ounces of a topical cream producing a 100mg/1.5 oz
30 solution. The patient applies the cream topically until a complete improvement is effected.

EXAMPLE 7

A method for diagnosing a skin disease as atopic dermatitis

Since many skin diseases have similar symptoms, a method of diagnosing a skin disease as
atopic dermatitis and, thus, identifying it as a disease which would be effectively treated with an
35 anti-mycoplasma agent is presented. The method involves the identification of the presence of

mycoplasma in the effected area. Skin cells from the area are scraped off and stained with acridine orange. The presence of mycoplasma is determined by microscopically examined using a fluorescence microscope fitted with an FITC filter set. Some of the white blood cells and, in particular, the red blood cells from the smear are stained. The stain appears as small dots over the surface of the cells, typical of a mycoplasma infection.

5

Other embodiments of the invention can be envisioned within the scope of the following claims.

WHAT IS CLAIMED IS:

1. A method for the treatment of atopic dermatitis in a mammal comprising the steps of:

administering to the mammal a pharmaceutical composition comprising an anti-mycoplasma agent in an amount effective to reduce or stop the symptoms of atopic dermatitis.

2. The method of Claim 1 wherein said administration is topically.

3. The method of Claim 1 wherein said administration is systemically.

4. The method of Claim 1 wherein said anti-mycoplasma agent is selected from the group consisting of: inhibitors of protein synthesis, inhibitors of nucleic acid synthesis, agents that injure the cell membrane, and agents that inhibit a metabolic function.

5. The method of Claim 4 wherein said anti-mycoplasma agent is selected from the group consisting of: doxycycline, erythromycin, polyenes, polymyxins, amphotericin B, colistin, imidazoles, Nystatin, Polymyxins, Chloramphenicol, Erythromycin, lincomycins, aminoglycosides, Amikacin, Gentamicin, Kanamycin, Neomycin, Netilmicin, Streptomycin, Tobramycin, Nalidixic acid, Novobiocin, Pyrimethamine, rifampin, Sulfonamides, azithromycin, clarithromycin, moxifloxacin, trovafloxacin, enrofloxacin, levofloxacin, ofloxacin, ciprofloxacin, fleroxacin, clinafloxacin, josamycin, tylosin, spiramycin, kitasamycin, kanamycin, toxithromycin, dirithromycin, chloramphenicol, thiamphenicol, tiamulin, oxytetracycline, chlortetracycline, grepafloxacin, Trimethoprim, (S)-(-)-9-fluoro-2,3-dihydro-3-methyl-10-[4-(2-pyridyl)-1-piperazinyl]-7H-pyrido[1,2,3-de][1,4]benzoxazine-6-carboxylic acid (YH-6), and Gatifloxacin.

6. The method of Claim 2, wherein the composition further comprises an agent selected from the group consisting of: Vitamin C, vitamin E, retinoic acid, sun screen, hydrocortisone, carnosine and anti-oxidants.

7. The method of Claim 2 wherein said dosage comprises administering an effective amount of more than about 10 mg/1.5 ml of the pharmaceutical two times daily until symptoms disappear.

8. The method of Claim 7 wherein said dosage comprises administering an effective amount of more than about 50 mg/1.5 ml of the pharmaceutical two times daily until symptoms disappear.

9. The method of Claim 8 wherein said dosage comprises administering an effective amount of about 100 mg/1.5 ml of the pharmaceutical two times daily until symptoms disappear.

10. The method of Claim 4 wherein said anti-mycoplasma agent is selected from the group consisting of: an aminoglycoside, a tetracycline derivative, an aminocyclitol, and a macrolide.

11. The method of Claim 2 wherein said effective amount is enough to cover the effected area.

12. The method of Claim 11 wherein said effective amount is 100 μ l to 300 μ l.

13. The method of Claim 7 wherein said pharmaceutical is doxycycline.

5 14. A method of diagnosing a skin disease as atopic dermatitis, comprising identifying the presence of mycoplasma in the affected area.